Computations between Metallocalix[4]arene Host and a Series of Four Oil-Based Fuel Pollutant Guests

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Abstract

Calculations using PM3 and mechanics methods on metallocalix[4]arene hosts **(1-10)** and substituted dibenzothiophene guests (A-D), which are generally known as oil-based fuel pollutants, show that host-guest formation is energetically favored. Calculations have been carried out for both 1/1 and 1/4 ratios of host/guest. There is no direct bonding between the metal center of the host and the sulfur of the guest in the host-guest complex. Sterically hindered dibenzothiophene guests show similar energies to the unhindered analogs. For calix[4]arenes **(5-10)** in partial cone conformations and having hydrogen rather than *p-tert*-butyl groups on the wide rim, host-guest formation occurs within the narrow rim rather than the wide rim. Host-guest association appears to occur *via* π-π interactions between host and guest phenyl groups rather than *via* metal-sulfur bonding. The study has importance especially in oil refining to obtain environmentally safe fuel oils and help supramolecular chemists in designing and synthesizing more sophisticated host molecules for the removal of sulfur from crude oil / refinery oil.

Keywords: *Calixarene, Dibenzothiophene, Host-Guest formation, Methyl mercury, Metallocalixarene, Supramolecular Chemistry.*

Introduction

The continued use of oil-based fuels for transportation places ever-increasing environmental demands on the producer of these fuels. One of these demands is meeting future environmental requirements by the production of ultraclean fuel. A challenge that remains in producing such fuels is the removal of the final traces of sulfur. This element needs to be absent because the combustion of sulfur-containing compounds results in the formation of environmentally unacceptable sulfur dioxide. One group of sulfur-containing compounds that is present in oil-based fuels is dibenzothiophenes. These compounds are particularly problematic for removal by hydrodesulphurization when they contain functional groups that sterically inhibit the

sulfur atom from approaching the catalyst surface [2]. Two alternate strategies that have been considered involve either a chemical method where an initial step is the insertion of a metal center into the carbon sulfur bond of the dibenzothiophene [3,4] or a biochemical degradation using *Rhodococcus erythropolis* KA2-5-1 [5]. An alternate approach to either of these two is solvent extraction [6] or to encapsulate the dibenzothiophene within a host molecule. A calixarene is a potential host for dibenzothiophenes. Furthermore, since calixarenes are conformationally mobile, they can be readily incorporated into sensor systems that are both analytically selective and sensitive [7, 8].

Calixarenes are cyclic oligomers obtained by a condensation reaction between *p-tert*-butylphenol and formaldehyde. Calixarenes are like crowns in that they are pre-organized complexants for metal ions. Unlike porphyrins, however, calixarenes are not fully conjugated, and their three-dimensional structure leads to cavities within the molecular framework [9]. Calixarenes are conformationally mobile, and the extreme structures for the calix[4]arenes have been termed the cone (uuuu), the partial cone (uuud), the 1,3-alternate (udud) and the 1,2-alternate (uudd) conformation [10-12]. Each of these conformers can act as a host molecule to uncharged aromatic molecules as guests [13-16], and each has a cavity within both the wide and the narrow rim. Because of the conical geometry of the calix[4]arene structure, the volume of the wide rim cavity is greater than that of the narrow rim [9]. By appending sulfur functionalities onto calix[4]arenes, metal ions such as mercury(II) have been complexed onto both of these rims [17-21].

Metallocalixarenes are potentially useful hosts for thiophenes because, in addition to having wide and narrow rim cavities that are compatible with an aromatic hydrocarbon, they also have a metal center that can coordinate to the sulfur. Mercury has a strong affinity for binding to sulfur, therefore we have chosen a mercury calixarene complex in designing hosts for a substituted dibenzothiophene guest.
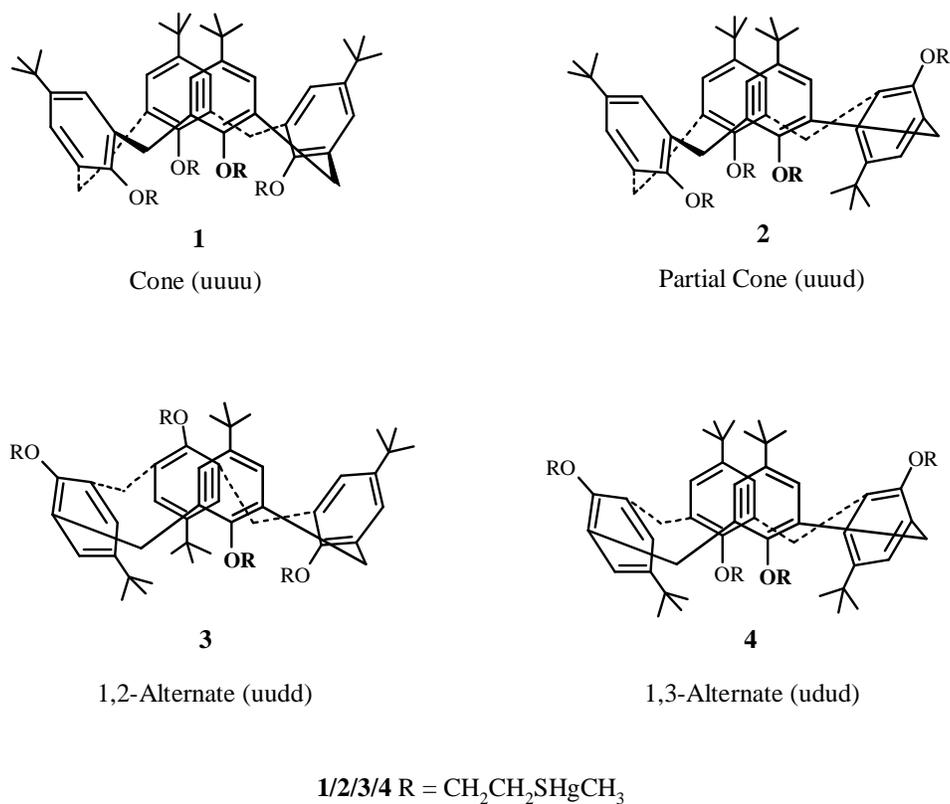
Recently we have reported the synthesis of a methylmercury(II) complexed calix[4]arene 1,2-ethoxythiolate [22], and carried out our initial computational studies on its function as a host for sulfur containing macrocyclic and heterocyclic guests [23]. These calculations were carried out on systems where the guest was bound *via* sulfur to the mercury(II) center on the calix[4]arene host. For substituted dibenzothiophenes, however, we need to occlude sterically hindered sulfur containing heterocyclic guests into a molecular host. This represents a different situation from unsubstituted heterocycles because hindered guest molecules may be sterically constrained from having direct mercury(II)-sulfur bonds between the host and guest.

Results

This decision to computationally investigate dibenzothiophenes as guests is based on two considerations. The first is that sterically hindered 2, 9-disubstituted dibenzothiophenes (**C** and **D**) are among the sulfur-containing heterocyclic compounds that are the most difficult to remove from crude oil [24]. Consequently, host molecules that occlude them would be useful. Secondly, in our previous calculations it was a thiophene guest that showed endothermic binding to the host. Since thiophenes are known to bind only weakly to a metal center, further computational studies may reveal how they interact with metallocalix[4]arene hosts [25].

We have carried out a series of computations between metallocalix[4]arene hosts (**1-10**) and a series of four sulfur containing heterocyclic guests (**A-D**) having functional groups appended that have different steric requirements (Schemes 1 and 2). The calculations are allowed to minimize freely without any constraint being introduced to favor mercury(II)-sulfur interactions (Tables 1 and 2). A further set of calculations (Table 3) have been carried out where a metal center other than methylmercury(II) is bonded to the ethoxythiolate sulfur of the substituted calix[4]arenes **5-10** (Scheme 2). These are Ag, EuMe, UMe₃, FeMe, and CrMe. Each is uncharged, with the oxidation state being accommodated by methyl groups to make them comparable with the methylmercury(II) derivative. This group has transition metals, a post transition metal, a lanthanide and an actinide. These particular examples are chosen because they have a propensity to complex with unsaturated hydrocarbons or have high coordination numbers [26].

Calculations have been carried out on a DEC alpha computer system (433 MHz) using the SPARTAN Version 5.0.2 software package [27]. This package is chosen because it has the algorithms available for heavy metals. All calculations have been carried out using PM3 (Setup: semi-empirical; Solvent: none; Total

1

Cone (uuuu)

2

Partial Cone (uuud)

3

1,2-Alternate (uudd)

4

1,3-Alternate (udud)

1/2/3/4 R = CH$_2$CH$_2$SHgCH$_3$

Scheme 1. Representation of metallocalix[4]arene host in different conformations

A

B

C

D

5 M = HgCH$_3$
6 M = Ag
7 M = EuCH$_3$
8 M = U(CH$_3$)$_3$
9 M = FeCH$_3$
10 M = CrCH$_3$
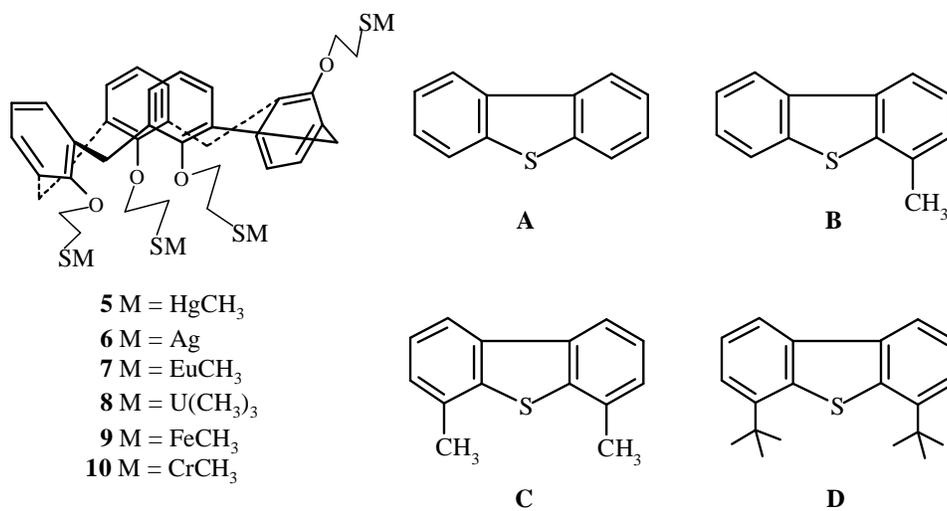
Scheme 2. Representation of metallocalix[4]arenes (5-10) and a series of four sulfur containing heterocyclic guests (Dibenzothiophenes A-D).

charge: 0; Multiplicity: singlet; Geometry: Merck), mechanics (Force field: Merck), and Density Functional Theory (Theory: SVWN; Basis: DN; Multiplicity: singlet; Total charge: 0) geometry optimization. The semi-empirical molecular orbital (PM3) method is based on a simplified Hartree-Fock model. The method is chosen because it is successful for calculating equilibrium geometries.

Table 1. Calculated Energies (PM3)[a] of the Metallocalix[4]arene (1-4) Hosts with Dibenzothiophene (A,B,C,D) Guests.

Adduct	S	B	ΔE[b]	L[c]
1/A	507.5	469.6	37.9	6.02
1/B	519.2	488.1	31.1	4.46
1/C	534.3	495.4	38.9	4.63
1/D	687.5	652.3	35.2	4.98
2/A	482.9	447.8	35.1	4.55
2/B	485.5	446.5	39.0	4.78
2/C	502.4	472.3	30.1	4.90
2/D	654.7	623.3	31.4	4.97
3/A	456.8	413.1	43.7	5.73
3/B	464.4	435.1	29.3	4.56
3/C	483.9	457.8	26.1	5.72
3/D	648.0	602.8	45.2	5.43
4/A	441.9	418.2	23.7	4.41
4/B	464.3	428.6	35.7	5.74
4/C	493.5	441.1	52.4	6.18
4/D	624.1	590.5	33.6	4.91

[a]Calculated Energies (PM3) of Separated (**S**); Bound (**B**); 1/4 adducts (**ΔE**[b]);
[b]ΔE is in Kcal mol^{-1}.
[c]Calculated Bond Length Shortest Hg-S (**L**[c]) is in Å.

A limitation is that the method can be less successful for ground-state conformations and conformational energies in cyclic systems. The density functional theory (SVWN/DN) method performs as well or better than limiting Hartree-Fock models for calculating equilibrium geometries. This method is a useful one for larger molecules, and is a good compromise in terms of

computational time. A limitation is that heavy-atom bond lengths are 0.2-0.3 Å shorter than experimental values. All reasonable conformations have been computationally searched before the one with the minimum energy was chosen. For the dibenzothiophenes (**A-D**), where there is little conformational flexibility, the energy minimum is quickly and reproducibly obtained by convergence. For the metallocalixarenes (**1-10**), however, more structural variations are possible. The primary conformation (uuuu etc) is determined by the initially chosen conformational representation of the calixarene structure, and the convergence minimum for that particular structural variation is then obtained. Usually the energy minimum is obtained for this predetermined primary conformation, and there is no crossover into the other conformations. The analogous energy minima for the other three conformations are similarly obtained. After the four separated dibenzothiophene and metallocalixarene combinations have been reproducibly minimized in energy, the graphical representation is modified to place the guest molecule (dibenzothiophene) in close proximity to the host (metallocalixarene). Upon commencing the minimization routine the guest molecule either moves away from the host cavity or it is attracted into it. In the latter case, the energy of the host-guest pair is lower than the separate entities.

Table 2. Calculated Energy changes (PM3) of the 1/1 Host-Guest Adducts of Metallocalix[4]arenes (1-4) with Sterically Hindered Dibenzothiophenes (C and D).

Adduct	ΔE*	Adduct	ΔE*
1/C	0.0	1/D	2.3
2/C	12.5	2/D	9.0
3/C	8.0	3/D	11.9
4/C	9.9	4/D	5.6

*ΔE is in Kcal mol^{-1}.

The 1/1 (host/guest) adducts have all been investigated in this manner. In no case did we find an attractive interaction when we placed the dibenzothiophene in the vicinity of the wide calixarene rim. The computational energies and

intermolecular separations for the host-guest systems that we have calculated are collected in Tables 1-3. Pair-wise calculations have been made for both the bound and unbound combinations among these compounds, and calculations have been carried out with both one (Table 2) and four (Table 1) dibenzothiophenes associated with the methylmercury(II) substituted calix[4]arene. For comparison, calculations have also been carried out on hypothetical derivatives having metals other than mercury(II) appended to the thiolate sulfur (Table 3). In each calculation the energy minimum is sought for each system investigated.

In our previous publication [23] we reported on calculations with both 1/4 and 1/1 ratios of the methylmercury(II) complexed calix[4]arene to an unsubstituted thiophene. In that study we observed an energy lowering $<\Delta E$ when the four thiophenes were brought into close contact with the calix[4]arene. We have now extended this study to dibenzothiophene (**A**) and its sterically hindered derivatives (**B-D**). Furthermore, we have also investigated all four conformations of the metallocalix[4]arene (**1-4**).

In our previous publication we assumed that the host-guest interaction was between the mercury atom of the host and the sulfur atom of the guest, although thiophene sulfur does not have an electron pair available for coordination to a metal. With sterically hindered dibenzothiophenes (**B-D**), mercury(II)-sulfur interactions are even less likely, so we have investigated further the source of the host-guest interaction.

Table 3. Calculated Energies and Bond Distances in 1/1 Host-Guest Adducts of Metallocalix[4]arenes (5-10) and Dibenzothiophene (A).

Host	ΔE^* (PM3)	ΔE^* (Mech)	ΔE^* (DFT)	$(Ph\text{-}Ph)^*_{min}$ (PM3)	$(Ph\text{-}Ph)^*_{min}$ (Mech)	$M\text{-}S^*$ (PM3)	$M\text{-}S^*$ (Mech)
5	19.79	11.89	14.11	4.75	4.74	5.89, 17.06, 5.82, 5.34	5.87, 17.10, 5.80, 5.31
6	----	13.62	13.28	----	4.63	----	17.46, 5.59, 6.25, 5.74
7	----	13.86	17.74	----	4.71	----	17.53, 13.70, 6.05, 5.51
8	----	17.57	13.36	----	5.05	----	15.55, 6.28, 5.60, 8.92
9	22.71	22.71	21.58	4.48	4.47	16.79, 6.19, 4.60, 5.84	16.77, 6.19, 5.64, 5.84
10	17.45	16.88	7.18	5.20	5.09	5.56, 14.21, 6.54, 12.09	5.55, 16.38, 5.51, 12.11

*Distances Ph-Ph and M-S are in Å and ΔE is in Kcal mol^{-1}.

Discussion

The computational energy data are collected in Tables 1-3. The data in Table 1 are for the methylmercury(II) complex in each of the four different conformations (uuuu, uuud, uudd, udud), and the four different dibenzothiophenes (**A-D**). These calculations using PM3 have been carried out with the methylmercury(II) complex and the dibenzothiophene in a 1/4 ratio. This 1/4 ratio corresponds to one dibenzothiophene molecule for each of the four methylmercury(II) centers in the complex. These calculations show there is an exothermic interaction (positive Δ) between the host and guest, even for the most sterically hindered benzothiophene (**D**) having *tert*-butyl groups in the 2,9-positions. Thus in each case, the adducts have lower computational energies than do the separated pairs. The energy differences ΔE show no significant discrimination between the groups of dibenzothiophenes (**A-D**) investigated. Column L in Table 1 lists the shortest distance between a mercury(II) and the dibenzothiophene sulfur in each minimized structure. In no case did we find that a sulfur of a dibenzothiophene guest is close enough to a mercury atom (L, 3.5 Å) to have any interaction. Apparently the positive values for ΔE are not the result of any mercury(II)-sulfur interactions between the host and guest, even for the sterically unhindered dibenzothiophene (**A**). This result is in agreement with experimental observations that thiophene only weakly complexes with metals [25].

In our previous calculations [23] with thiophene as the guest we found that although there was a positive interaction ΔE between the host and guest when they were in a 1/4 ratio, there was not when the ratio was 1/1. We suggested that this difference could be a consequence of favorable guest-guest interactions in the former case.

In order to eliminate the possibility that positive values of ΔE are a result of guest-guest interactions, we have further investigated the most sterically hindered guests **C** and **D** in a 1/1 ratio of host to guest. In Table 2 are collected these potential energy data. Again, no steric discrimination is discernible. Both **C** and **D** give similar values for ΔE with all four conformers

(**1-4**). The most disfavored conformation for host-guest formation, however, is the cone (**1**). This is not an unexpected result because the cone conformation places the most restrictions on the guest molecule in terms of how it can fit into the cavity. There is no obvious explanation, however, why the value of ΔE is larger for the more sterically hindered combination **3/D** than it is for **3/C**.

In order to try and better understand the host-guest interactions in these combinations we have minimized the steric interactions. In Table 3 are collected the computational energy differences for 1/1 host-guest adducts between the dibenzothiophene **A** and an analogous calix[4]arene host having hydrogens rather than *tert*-butyl groups in the *para*-positions. The elimination of the sterically bulky *tert*-butyl groups on the wide rim of the calix[4]arene potentially allows for host-guest formation to occur in either the wide or narrow rim cavities. Also, in order to determine whether host-guest formation is uniquely due to the methylmercury(II) substituent, we have carried out calculations with different metal centers. We have therefore concentrated our host-guest formation studies only between **A** and the partial cone (uuud) conformer of all the metallocalix[4]arenes (**5-10**). In each case for M = $HgCH_3$, Ag, $EuCH_3$, $U(CH_3)_3$, $FeCH_3$, and $CrCH_3$, the guest dibenzothiophene (**A**) is repelled rather than attracted by the wide rim cavity, resulting is unfavorable energies. By contrast, favorable energies are observed for the narrow rim, and the dibenzothiophene guest is encapsulated within the minimized structure. This result is reflected in positive values for ΔE (Table 3). Again there is no close interaction between the sulfur of the dibenzothiophene guest and the metal center (M-S) of the calix[4]arene host. The shortest such separation is 4.60 Å. Because there is a possibility that the positive ΔE values result from a host-guest attraction that involves π-π interactions between phenyl groups on the host and guest, we have computationally estimated the distances between the centers of the phenyl groups of the metallocalixarene host and the guest **A** in each minimized structure. Since there are four phenyl groups on the host that can interact with the pair of phenyl groups of **A** that is now in the cavity, it is

necessary to determine eight phenyl-phenyl separations for each host-guest adduct. Since many of these phenyl-phenyl separations are too large to be significant we are only reporting the shortest one in each case, because this will be the best indicator as to whether these phenyl-phenyl interactions may play a role in host-guest adduct formation. The shortest of these distances range from 4.48 for M = $FeCH_3$, to 5.25 Å for M = $EuCH_3$. With **A** interacting with the host through a phenyl group, the sulfur atom of **A** approaches a distance to the metal M somewhat longer. We recognize that these distances are long, and that none of them are sufficiently short that they can make a dominant contribution to the host-guest attraction. Instead, the overall attraction appears to be the sum of several very weak forces. The metal-sulfur (M-S) distances in Table 3 show two types of host-guest formation. For M = $HgCH_3$, $U(CH_3)_3$, and $FeCH_3$ there are three short and one long distance, but for M = $EuCH_3$ and $CrCH_3$ there are two short and two long distances. For M = Ag both types are observed depending on the computational method used. At least one long distance is to be expected, because the partial cone conformation places one metal center a long distance away from the narrow rim cavity. For cases with three short distances the guest sulfur is close to being equidistant from the three metals, but for those with only two short distances, the sulfur is only symmetrically close to two metals. The energy differences between these two idealized conformations is small, which is reflected in PM3 and mechanics giving different answers in one case, and in the case of M = $U(CH_3)_3$ which has an intermediate conformation for the host-guest complex. We recognize that in molecules of this size and complexity with heavy metals present there are many possible conformations, so we only consider large differences in energy as being significant, and we make no attempt to rationalize small energy differences.

Conclusion

The study emphasized here elaborates the importance of computational methodology in constructing model host molecules for targeted guest species. The calculations made show that there is a weak interaction between metallocalixarene hosts and dibenzothiophene guests. Metal-sulfur interactions make minimal contribution to the energies of attraction. The presence of sterically bulky substituents on the dibenzothiophene does not inhibit host-guest formation. Host-guest formation preferentially occurs at the narrow rim of the calix[4]arene host, which is the one having the greatest volume and conformational flexibility. However, the factors other than metal-sulfur interactions may also help in designing a host molecule for the removal of sulfur containing pollutants from oil based fuels. These results suggest that metallocalixarenes may be useful hosts for trapping dibenzothiophenes, even when complexation with the sulfur atom is sterically blocked.

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